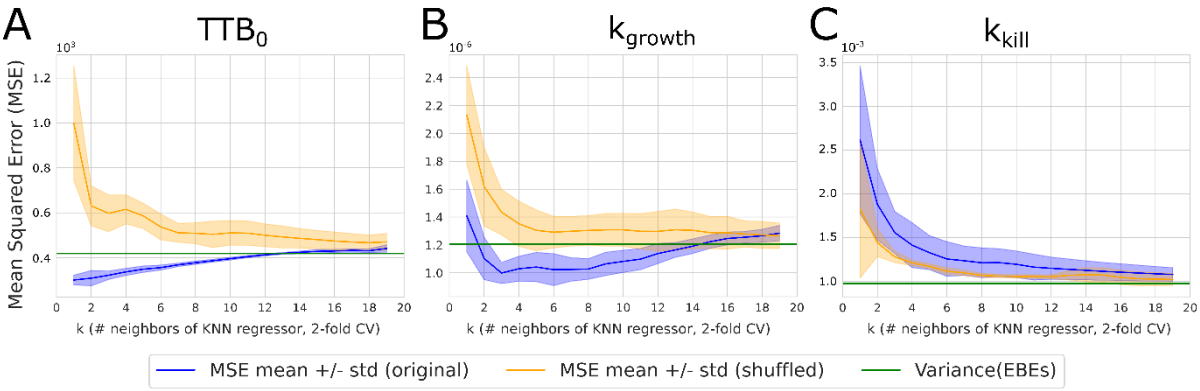
Supplementary material 3: Results of global assessment step (step 0) of the radiomics covariate selection process to investigate whether radiomics feature sets provide predictive information for most probable parameter estimates (EBEs) of one of the model parameters. Subfigures show the Mean-Squared Error (MSE) of k-Nearest Neighbor (kNN) prediction models for the EBEs for (A) TTB0, (B) kgrowth and (C) kkill as a function of the number k of nearest neighbors used for prediction. The green line indicated the variance of the EBEs.



For k approaching the number of patients N (38 patients, 2-fold cross-validation: N=19), the MSE converges to the sample variance of the respective model parameter EBEs (green line). In the absence of predictive information in the radiomics dataset, the best kNN prediction is obtained when using the largest possible number of nearest neighbors (N-1) to predict the EBE of the N-th patient. The variance (VAR) of the EBEs then constitutes a lower limit for kNN prediction performance. If, on the other hand, the radiomics dataset does provide predictive information, a lower MSE (MSE<VAR) will be achieved for one or more values of k.

Subfigures (A) and (B) illustrate this pattern for model parameters TTB0 and k_{growth}: the MSE for EBE prediction based on the original radiomics dataset (blue line) is consistently lower than the MSE for prediction using a shuffled copy of the radiomics dataset (orange) in which the relation between radiomics features and model parameter EBEs had been randomized. In contrast, for the prediction of model parameter k_{kill}, both original and shuffled datasets perform similarly with MSEs consistently exceeding the variance of the outcome dataset.